International Society of Gastrointestinal Oncology
2009 Gastrointestinal Oncology Conference
October 1–3, 2009

ABSTRACTS SELECTED FOR POSTER PRESENTATIONS

Gastrointestinal Malignancies—General

abstr 0961

Nigella sativa L Oil Ameliorates Methotrexate-Induced Intestinal Toxicity

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Backgound: The efficacy of methotrexate (MTX) chemotherapy is often limited by side effects, the mechanism of which is via oxidative stress. In this study, *Nigella sativa* L (*N. sativa)* oil, a natural antioxidant, was studied as a protective agent against MTX-induced intestinal toxicity via its antioxidant activity.

Materials and Methods: A total of 24 male albino rats were divided into four groups as follows: group 1, saline control; group 2, *N. sativa* oil (10 mL/kg); group 3, saline interrupted on day 6 by MTX (20 mg/kg, IP single dose); and group 4, *N. sativa* oil and MTX given on day 6. In the two groups injected with MTX, blood samples were collected at time intervals (0, 1, 3, 4, 5, and 24 hours) to determine serum MTX levels. On day 10, blood samples were collected from the four groups for hematologic assessment of hemoglobin (Hb%), RBCs, WBCs, and platelets. All rats were then sacrificed; sections from intestine and liver were cut and homogenized for biochemical analysis, measuring glutathione (GSH) content and superoxide dismutase (SOD) activity. Also, sections from intestine, liver, and kidney were removed for pathologic examination after staining with H & E.

Results: Food consumption increased in the *N. sativa* group. Body weight loss in the *N. sativa* oil plus MTX–treated group compared with the MTX group was 12.7% vs. 29.4 % ($P < .05$). Moreover, severe degeneration of the intestinal mucosa, liver parenchyma, glomerular, and tubular epithelium observed in the MTX-treated group was improved by *N. sativa* oil treatment. Parallel to these results, *N. sativa* oil resulted in a significant decrease in SOD content, which was elevated by MTX ($P < .05$); whereas GSH content in the MTX group was decreased by 53% compared with that in the MTX plus *N. sativa* oil group ($P < .05$). The addition of *N. sativa* oil did not significantly change MTX level ($P > .05$), ruling out drug

interaction. Furthermore, *N. sativa* oil significantly increased total RBCs, WBCs, as well as Hb% ($P < .05$) compared with MTX, but did not cause a significant change in platelet count ($P > .05$).

Conclusion: Administration of *N. sativa* oil before and after MTX injection ameliorated MTX-induced gastrointestinal toxicity and maintained mucosal structure through its anti-oxidant activity. These results can lead to further clinical applications for prevention of chemotherapy-induced gastrointestinal toxicities.